AO 120 (Rev. 2/99)

TO:	
Commissioner of Patents **P.O. Box 1450** **Alexandria, VA 22313-1450**	**REPORT ON THE FILING OR DETERMINATION OF AN ACTION REGARDING A PATENT OR TRADEMARK**

In Compliance with 35 § 290 and/or 15 U.S.C. § 1116 you are hereby advised that a court action has been filed in the U.S. District Court Colorado on the following Patents

DOCKET NO.	DATE FILED	U.S. DISTRICT COURT
11-cv-01389-WJM-MEH	**May 25, 2011**	**FOR THE DISTRICT OF COLORADO**
PLAINTIFF GENETIC TECHNOLOGIES LIMITED		DEFENDANT AGILENT TECHNOLOGIES, INC., et al

PATENT OR	DATE OF PATENT	HOLDER OF PATENT OR TRADEMARK
1 5,612,179		**Please see copy of Complaint attached hereto**
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In the above—entitled case, the following patent(s) have been included:

DATE INCLUDED	INCLUDED BY ☐ Amendment ☐ Answer ☐ Cross Bill ☐ Other Pleading	
PATENT OR	DATE OF PATENT OR TRADEMARK	HOLDER OF PATENT OR TRADEMARK
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In the above—entitled case, the following decision has been rendered or judgement issued:

DECISION/JUDGEMENT

CLERK	(BY) DEPUTY CLERK	DATE
GREGORY C. LANGHAM		

Copy 1—Upon initiation of action, mail this copy to Commissioner Copy 3—Upon termination of action, mail this copy to
Copy 2—Upon filing document adding patent(s), mail this copy to Commissioner Copy 4—Case file copy

spectrometry, microarrays, polymerase chain reaction (PCR) instrumentation, related bioreagents, electrophoresis, laboratory automation and robotics, software and informatics, nuclear magnetic resonance (NMR) and magnetic resonance imaging (MRI) systems, and related consumables and services." Many of the Agilent products responsible for these revenues utilize methods that infringed upon claims of the '179 Patent.

31. By way of example only, the Agilent 2100 Bioanalyzer has been used to determine a single nucleotide polymorphism, specifically the G20210A mutation, which is in a non-coding region of the prothrombin gene and results in a hereditary predisposition to venous thrombosis. In practice, DNA is amplified using PCR and analysis of the DNA is conducted using RFLP and the 2100 Bioanalyzer. These activities infringed at least one claim of the '179 Patent.

32. Also, by way of example only, Agilent's GeneSpring Analysis Platforms have also been used to infringe at least one claim of the '179 patent when used to analyze DNA in the non-coding region. For instance, GeneSpring GT "enables you to quickly identify genotype-phenotype relationships using a comprehensive set of linkage and association algorithms." GeneSpring GT has also been used to identify non-coding markers which provide useful information concerning linked DNA.

33. Also, by way of example only, Agilent has offered for sale a range of Comparative Genomic Hybridization Microarrays that have been used to infringe at least one claim of the '179 Patent. These microarrays enable characterization of genetic variations, including those caused by developmental abnormalities, disease susceptibility and differential drug responses. For example and upon information and belief, Agilent has offered for sale HD-

CGH Custom Arrays, where genes may be amplified using PCR and probes include both coding and non-coding sequences on the chromosomes to be analyzed.

34. Upon information and belief, Agilent had actual knowledge of the '179 Patent during times relevant to this action through at least its research, development and/or patent application activities.

B. BRISTOL-MYERS

35. Bristol-Myers is actively engaged in pharmacogenetics. Bristol-Myers claims that it: "engages in genomic research for the purpose of improving human health care, and we endorse an open and informed public dialogue on all aspects of genomic research. . . . At Bristol-Myers Squibb, we currently use biomarkers in most of our first-in-human studies. Pharmacogenomic studies, which combine traditional pharmaceutical sciences such as biochemistry with annotated knowledge of genes, proteins and single nucleotide polymorphisms, are run in nearly all our oncology projects to more precisely target patient populations. . . . Bristol-Myers Squibb's bioinformatics group exploits and integrates all available sources of genome data to understand disease, for use throughout the drug discovery process."

36. Bristol-Myers is a member of the Industry Pharmacogenomics Working Group, a voluntary and informal association of pharmaceutical companies engaged in research in the science of pharmacogenomics. Bristol-Myers is also a member of The SNP Consortium (the "TSC"). According to TSC marketing materials: "The goal of the TSC allele frequency/genotype project is to determine the frequency of certain SNPs in three major world populations . . . to enhance the understanding of disease processes and facilitate the discovery and development of

safer and more effective medications." Given that the majority of the human genome is covered by the non-coding region, many of these SNPs are located in non-coding regions.

37. Bristol-Myers has also actively advocated pharmacogenetic research and has undertaken its own studies and has supported third party studies via grants and funding. These studies support Bristol-Myers' investigations of gene polymorphisms associated with disease and drug response.

38. Bristol-Myers' pharmacogenetic activities include the analysis of non-coding DNA markers. By way of example only, and upon information and belief, Bristol-Myers has analyzed (or directed others to analyze) non-coding markers in connection with its Coumadin (Warfarin) and Plavix (Clopidegral) drugs using methods that infringe the '179 Patent. These Bristol-Myers products received label changes to reflect pharmacogenomic information in 2007 and 2009, respectively.

39. Warfarin is the most widely prescribed anticoagulant for thromboembolic therapy in North America and Europe. Approximately 2 million people are initiated on Warfarin therapy each year to prevent blood clots, heart attacks and stroke. However, Warfarin dosage requirements are highly variable both inter-ethnically and inter-individually. Mutations in vitamin K epoxide reductase complex, subunit 1 (VKORC1) have been identified to be associated with Warfarin effect and dosage. According to the FDA's adverse events reporting database: "complications from Warfarin (Bristol-Myer's Squibb's Coumadin) are the second most common reason for patients to go to the emergency room. . . ." Thus the use of pharmacogenetic testing is very important to the safety and efficacy of Coumadin. Coumadin is a commercially available form of Warfarin registered to Bristol-Myers Squibb Pharma Company, a division of

Bristol-Myers. There is currently, and has been for some time, no direct competitor drug to Coumadin on the market.

40. A polymorphism in the promoter region of VKORC1 gene, -1639 A>G, is highly associated with inter-individual variability in Warfarin dose requirements. Promoter polymorphism -1639 A>G is listed by the FDA as a bio-marker for pharmacogenomic testing for Warfarin sensitivity. It is claimed that 30% of dosage variability in Caucasian population is attributed to the VKORC1 gene alone.

41. In 2007, Bristol Myers began including information about the importance of -1639 A>G and Warfarin dosage in the package insert of Coumadin. The importance of the VKORC1 genotype in deciding the initial dosage is also emphasized in the inserts. In 2009, the International Warfarin Pharmacogenetics Consortium (IWPC) developed a Warfarin dose prediction algorithm using findings from nine different countries and based on the relationship between dose requirements and the known clinical and genetic factors.

42. There are four FDA approved tests (Nanosphere, Autogenomics, ParagonDX and Osmetech) available for Warfarin testing. In addition, numerous laboratory developed test are also available. The first genetic test to be cleared by the FDA for Warfarin resistance testing was Nanosphere's genetic test. The test was cleared in September 2007, shortly following Bristol-Myers' labeling change for Coumadin.

43. Upon information and belief, Bristol-Myers has (and/or has direct others to) amplify DNA with a primer pair spanning a DNA sequence containing the -1639A>G polymorphism which Bristol-Myers has associated with inter-individual variability in Warfarin

dosage requirements. The analysis of this non-coding DNA marker in this manner thus infringed upon claims of the '179 Patent.

44. With respect to Clopidegral, its metabolism is enhanced by CYP2C19*17 promoter polymorphism -806 C>T. Bristol-Myers has funded and/or provided assistance to several studies to investigate the impact of genetic polymorphisms on metabolism of Clopidegral, with at least two such studies analyzing the non-coding CYP2C19*17 promoter polymorphism.

45. Plavix, Bristol-Myers' commercially available form of Clopidegral, is Bristol-Myers' largest selling drug, accounting for $6.7 billion sales in 2010. This drug is marketed by Bristol-Myers along with Sanofi-Aventis.

46. In March 2009, the FDA announced a new Plavix warning alerting doctors and patients to the effectiveness of Plavix depending on CY2C19 genotype. Enhanced metabolisers carry CYP2C19*17 allele, which is a promoter polymorphism (-806 C>T). This non-coding promoter polymorphism is not included in the Plavix package insert, however it is included in the genetic tests offered by laboratories to test effectiveness of Clopidegral.

47. Upon information and belief, Bristol-Myers has (and/or has direct others to) amplify DNA with a primer pair spanning a DNA sequence containing the -806 C>T polymorphism which Bristol-Myers has associated with metabolism of Clopidegral. The analysis of this non-coding DNA marker in this manner thus infringed upon claims of the '179 Patent.

48. Bristol-Myers has also performed (and/or directed others to perform) other genotyping activities that infringed one or more claims of the '179 Patent. Upon information

and belief, these activities were also directly related to the safety and efficacy and thus the development and/or sale of various drugs.

49. By way of example only, Bristol-Myers conducted a study in 2008 (by Ranade et al.), to study the role of genetic variation associated with highly active antiretroviral therapy. The study investigated almost 300 SNPs in 135 candidate genes. The study genotyped "the entire cohort for eight SNPs in resistin, including four newly identified by sequencing and two from phylogenetically conserved regions." Some of these SNPS were in non-coding regions. It was determined in the study that "none was as significantly associated as the SNP in intron 2. . . . Furthermore, haplotype analysis revealed that only haplotypes bearing the intron 2 SNP, rs3219177, were significantly associated with cluster membership. . . . Taken together these results indicate that this SNP is potentially causative." This study was related to HIV treatment. Bristol-Myers claims that it: "has long been a leader in developing innovative HIV/AIDS medications and treatments and will continue to make HIV/AIDS research a top priority. . . . Our company allocates substantial R&D resources to developing new medicines and treatments in the global fight against HIV/AIDS. We are exploring new ways to attack the AIDS virus and new ways to help make treatments for patients to take."

50. Also by way of example only, Bristol-Myers conducted a study in 2007 (by Zhang et al.), involving PCR amplification of the UGTA1*28 polymorphism, to study characterization of the UDP glucuronosyl transferase activity of human liver microsomes genotyped for the UGT1A1*28 polymorphism.

51. Also by way of example only, Bristol-Myers funded a study in 2006 (by Florez et al.), concerning the association of two non-coding SNPs rs12255372 and rs7903146 of the

TCF7L2 gene with the progression to diabetes. Genotyping was performed in the study using allele specific primers.

52. Upon information and belief, Bristol-Myers had actual knowledge of the '179 Patent during times relevant to this action through at least its research, development and/or patent application activities.

C. ESTA

53. ESTA has facilities in Colorado and California and offers seed genetics, seed quality and plant health services to others. According to its literature, ESTA's "high-throughput DNA laboratory is located in [the] Colorado facility and is supported by a network of Eurofins DNA laboratories throughout the world."

54. ESTA genetic services consist of two divisions: "the HTP Lab which specializes in isoelectric focusing (IEF) of plant proteins for hybrid purity, varietal identification and uniformity and the DNA Lab which works with various types of DNA specific markers which encompasses everything from database applications to marker assisted selection, to screening with trait linked markers, GMO screening and more. . . . If a given hybrid turns out to be non-informative or monomorphic regarding the protein banding patterns we can then pass it on to our DNA lab which has about a 99% success rate in identifying polymorphisms in most vegetable species." ESTA's DNA Lab offers marker assisted backcrossing (MAB), marker assisted selection (MAS), database genotyping (DB), trait linked markers (TLM), and quantitative trait loci (QTL) identification services.

55. ESTA's marketing materials discuss commonly used molecular markers in the plant breeding industry. Among many desirable qualities for a marker, the top two desirable

qualities are polymorphic and multi-allelic. The two markers identified by ESTA as satisfying these criteria are PCR-based Simple Sequence Repeats (SSRs) and Single Nucleotide Polymorphism (SNPs).

56. The majority of SSRs are non-coding as a majority of the genome is non-coding.

57. The majority of SNPs will also be in a non-coding DNA region. Indeed, ESTA admits that: "SNPs are abundant in all genomes and can be found approximately every kilobase (1,000 base pairs). They are also spread evenly throughout the genome. This offers the potential for generating very high density genetic maps, which will be extremely useful for developing haplotyping systems for genes or regions of interest. They may be the polymorphisms associated with the gene of interest under study and therefore direct selection of the gene is possible."

58. ESTA admits that it has "identified an optimal number of markers spaced throughout a plant's genome and studied computer simulations to determine the number of plants to test each generation. In each backcross generation, the population has a wide range for percentage of recurrent parent genome. Applying DNA markers effectively and efficiently allows you to identify the individuals that inherit the highest percentage of the recurrent parent genome plus the trait of interest. As a complement after backcrossing, our service can select individuals homozygous for the trait of interest thereby expediting commercialization of your product."

59. Upon information and belief, ESTA has also customized marker strategies to suit customer needs and also analyzes markers to select desired traits and help design desired genetic ratio of original parent and cross as a part of its MAS services.

60. ESTA has also offered database genotyping which is based on "specific sets of molecular markers for any given species" and "use the same set of DNA markers on all entries." ESTA admits on its website that genotyping can be used for inbred line development, confirmation of pedigrees and association studies. ESTA also claims to have collected a large number of trait linked markers in many species. According to ESTA: "In some cases, we have identified molecular markers linked to genes which promote expression of a specific trait, for example a disease resistance gene. Using the marker, we can identify plants carrying the gene, including the zygosity, even in the absence of the selection agent and at any stage of plant growth."

61. Sometimes important traits are difficult to select by phenotype due to contribution by more than one gene or failure to locate a gene that is responsible for the trait. In such cases markers are used to map and identify a locus using appropriate phenotypic, genotypic and statistical analyses. A stretch of DNA containing the gene or linked markers responsible for a quantitative trait is referred to as a QTL. Upon information and belief, ESTA has offered QTL mapping and identification services by closely working with their customers "to determine the best population type to work with, number of individuals to test, number of markers to apply, and other unique aspects of your breeding program to help ensure you accomplish your program goals." ESTA also states that its "Genetic Services can identify DNA markers that span a plants genome based on your specific population(s). When analyzed on a segregating or recombinant inbred population along with appropriate phenotypic data, genomic regions can be identified which contribute to a specific phenotype. The phenotype or trait could be a quantitative trait implying many genes could contribute to the phenotype or a qualitative trait resulting from one

or two major genes." Trait specific molecular marker technology (MMT) is also used by ESTA genetic services laboratory to test hybrid purity.

62. U.S. Patent Application Publication No. U.S. 2011/0041204 A1, entitled "Methods for Enhancing the Production and Consumer Traits of Plants" ("the '204 Publication") refers to the use of ESTA services sometime before the filing date of the '204 Publication on August 12, 2009. The '204 Publication states: "Even if an enzymatic basis for a particular mutant gene is not known, and the nucleotide sequence for the gene encoding the enzyme is not known, and is not present in the Maize Genetics and Genomics or GenBank databases, the inheritance of the gene can still be determined by those having ordinary skill in the art by following nearby molecular markers on the chromosome including the gene. . . ." The '204 Publication also discusses the use of commercially available DNA polymorphisms that were tested for trait identification for the su1, se2 and sh2 genes. The sh2 gene, which is multi-allelic, can mutate from a G nucleotide to a C, T or A nucleotide in intron 15 of the gene. When the mutation (C, T or A) is expressed in a plant, such as maize, enhanced growth characteristics occur. The '204 Publication further states that ESTA provided services and used 330 SSR markers for the study described in the '204 Publication. All of those markers are, upon information and belief, in non-coding regions.

63. As described above, ESTA has utilized many non-coding DNA markers using amplified DNA with a primer pair spanning a DNA sequence containing these non-coding markers. For example, ESTA's marketing materials describe the laboratory process for seed sampling to include PCR amplification. ESTA has associated these markers with genes

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLORADO

Civil Action No. _____

GENETIC TECHNOLOGIES LIMITED,
an Australian corporation,

Plaintiff,

v.

AGILENT TECHNOLOGIES, INC., a Delaware corporation;
BRISTOL-MYERS SQUIBB COMPANY, a Delaware corporation;
EUROFINS STA LABORATORIES, INC., a Colorado corporation;
GLAXOSMITHKLINE PLC, a British company;
HOLOGIC, INC., a Delaware corporation;
MERIAL L.L.C., a Delaware limited liability company;
NAVIGENICS, INC., a Delaware corporation;
NEOGEN CORPORATION, a Michigan corporation;
PFIZER INC., a Delaware corporation; and
454 LIFE SCIENCES CORPORATION, a Delaware corporation;

Defendants.

COMPLAINT WITH JURY DEMAND

Plaintiff Genetic Technologies Limited ("GTG") files this Complaint against Defendants Agilent Technologies, Inc. ("Agilent"), Bristol-Myers Squibb Company ("Bristol-Meyers"), Eurofins STA Laboratories, Inc. ("ESTA"), GlaxoSmithKline ("GSK"), Hologic, Inc. ("Hologic"), Merial L.L.C. ("Merial"), Navigenics, Inc. ("Navigenics"), Neogen Corporation ("Neogen"), Pfizer Inc. ("Pfizer"), and 454 Life Sciences Corporation ("454") (hereinafter referred to collectively as "Defendants" unless otherwise specified) alleging as follows:

responsible for desired traits of economic importance. ESTA's analysis of these non-coding DNA markers thus infringed upon claims of the '179 Patent.

64. Upon information and belief, ESTA had actual knowledge of the '179 Patent during times relevant to this action through at least its research, development and/or patent application activities.

D. GSK

65. GSK is active in the area of pharmacogenetics. In its marketing materials it admits that: "GSK invests heavily in research, including genomic and genetic research, that may lead to . . . and new methods of disease detection, prevention and treatment."

66. GSK's 2005 Annual Report outlines how pharmacogenetics plays a role in the strategies used by GSK for drug development:

> Two components are needed in the early stages of finding new medicines - targets that can be shown to affect mechanisms of important pathological processes in human disease and compounds able to modulate the behavior of specific targets. Many diseases arise through complex interactions between gene variants and environmental factors. Within GSK, Genetics Research aims to take advantage of this by identifying genes which influence common diseases with large unmet medical needs and major patient burdens. These insights help in the search for targets with known relevance to the disease, and hence a greater chance of delivering benefit to the patients. Discovery Research (DR) produces the lead compounds that may influence targets which form the basis of drug discovery efforts in GSK's Centres of Excellence for Drug Discovery (CEDDs). In 2005, DR performed over 90 million assays and provided the CEDDs with 50 high-quality new lead compounds. Investment in DR has been focused on increasing the quality and quantity of the lead compounds available.

67. GSK also reports that it is "an active member of the SNP Consortium [TSC], a collaboration between industry and the UK's Welcome Trust, contracting with academic institutions to identify and map SNPs. The information arising from the collaboration is a valuable research tool and has been placed in the public domain without IP restrictions. GSK

believes that the value of SNPs lies not so much in their identification but in their association with diseases or patient response to medicines." As noted above, TSC marketing materials indicate that: "The goal of the TSC allele frequency/genotype project is to determine the frequency of certain SNPs in three major world populations . . . to enhance the understanding of disease processes and facilitate the discovery and development of safer and more effective medications." Given that the majority of the human genome is covered by the non-coding region, many of these SNPs are located in non-coding regions.

68. GSK has actively advocated pharmacogenetic research and has undertaken its own studies and has supported third party studies via grants and funding. These studies support GSK's investigations of gene polymorphisms associated with disease and drug response.

69. GSK's pharmacogenetic activities include the analysis of non-coding DNA markers. By way of example only, and upon information and belief, GSK has analyzed non-coding markers in connection with the drugs Ziagen (Abacavir) and Tykerb (Lapatinib) using methods that infringed the '179 Patent. These activities were related to the safety and efficacy and thus the development and/or sale of Ziagen and Tykerb.

70. Abacavir is an antiviral medication used in combination with other antiretroviral drugs for the treatment of HIV-1 infection. Ziagen is a commercially available form of Abacavir.

71. In 2005, GSK conducted a study to identify genetic markers associated with presence or absence of Abacavir hypersensitivity. Using a genome wide SNP genotyping approach including both coding and non-coding region, genes associated with immune response

72. Lapatinib is a tyrosine kinase inhibitor and is an oral medication for breast cancer. It inhibits HER2 and EGFR and is used in HER2 positive women with metastatic breast cancer. In a 2007 article in Pharmaweek, GSK's Allen Roses described the use of densely mapped SNPs within cytochrome P450, genes particularly in CYP2C19, that include non-coding polymorphisms. Some variants were associated with side effects to this drug. Upon information and belief, GSK has also conducted and/or funded at least two pharmacogenetic studies related to the use of Tykerb in the treatment of breast cancer.

73. Upon information and belief, GSK has (and/or has direct others to) amplify DNA with a primer pair spanning a DNA sequence containing non-coding polymorphisms which GSK has associated with the efficacy of Lapatinib. The analysis of this non-coding polymorphism in this manner thus infringed upon claims of the '179 Patent.

74. GSK has also performed (and/or directed others to perform) other genotyping activities that infringed one or more claims of the '179 Patent. Upon information and belief, these activities were also directly related to the safety and efficacy and thus the development and/or sale of various GSK drugs.

75. By way of example only, GSK conducted a study in 2009 that was reported in an article entitled "CTLA4 Gene Polymorphisms are Associated with Chronic Bronchitis" in the European Respiratory Journal. It was reported in the article that:

> Six CTLA4 SNPs were significantly associated with chronic bronchitis in the ICGN cohort ($0.0079 \leq p \leq 0.0432$) with three being replicated with the same directionality of association in the Bergen cohort ($0.0325 \leq p \leq 0.0408$). One of these replicated SNPs (rs231775) encodes the Thr to Ala substitution at amino

> acid position 17. Haplotype analyses supported the results of single SNP analyses . . .
>
> As CTLA4 is located near the region on chromosome 2q that showed significant linkage with COPD-related phenotypes both in the Boston Early-Onset COPD Study 9-11, as well as in general population pedigrees 12, we hypothesized that CTLA4 single nucleotide polymorphisms (SNPs) would be associated with COPD and COPD-related phenotypes, including the severity of airflow limitation and the presence of chronic bronchitis . . .
>
> Genotyping in the two cohorts was performed with the Illumina array-based custom SNP genotyping platform.
>
> We found significant associations with the other COPD-related phenotype investigated, chronic bronchitis. In the ICGN families, six out of the nine CTLA4 SNPs genotyped (SNPs rs926169, rs11571316, rs231775, rs231779, rs3084243 and rs231725) were significantly associated with the chronic bronchitis phenotype ($0.0079 \leq p \leq 0.0432$). Associations with SNPs rs231775 and rs3087243 ($p = 0.0081$ and 0.0079, respectively) were significant even after a correction for multiple testing. We replicated the significant association with chronic bronchiitic phenotype in the COPD cases of the Bergen cohort for four of the six CTLA4 SNPs (rs11571316, rs231775, rs3087243 and rs231725; $0.0325 \leq p \leq 0.0408$) identified in the ICGN study. After evaluating the risk allele, we found that three of the replicated significant SNPs (rs231775, rs3087243 and rs231725) for chronic bronchitis have the same directionality of association in the two populations.
>
> We did not detect any significant association with chronic bronchitis in control subjects without COPD in the Bergen cohort, suggesting that CTLA4 is associated with chronic bronchitis among COPD subjects . . .
>
> In the ICGN study, we identified two haplotype blocks. Several of the significantly associated SNPs (rs926169, rs11571316, rs231775 and rs231777) were located in block 1, while three other significantly associated SNPs (rs231779, rs3087243 and rs231725) were located in block 2.

Among the nine SNPs genotyped in the study, 8 are located in non-coding regions, namely rs926169 (5' intergenic region upstream of CTL4 gene), rs733618, rs11571316, rs16840252 located in the promoter region, rs231777, rs231779 located in the intron, rs3087243, and

rs231725 located downstream of the CTL4 gene. Upon information and belief, GSK has analyzed these SNPs in a manner that infringed upon claims of the '179 Patent.

76. Also by way of example only, GSK conducted a study in 2007 that was reported in an article entitled "Association of PTGDR Gene Polymorphisms with Asthma in Two Caucasian Populations" in the Genes & Immunity Journal. Therein it was reported that:

> The prostanoid DP receptor (PTGDR) is shown to be involved in the asthma patho-physiology and the results from the published genetic association studies are inconsistent. Four single nucleotide polymorphisms (SNPs) in PTGDR were genotyped in 342 and 294 families from UK and Denmark respectively. Asthma and asthma-related phenotypes were analyzed using family-based association analyses. In the UK families, a promoter polymorphism (-731A/G) showed significant associations with asthma (P=0.0022), atopic asthma (P=0.0044), bronchial hyper reactivity or BHR (P=0.00120) and strict asthma (P=0.0008). The p-values for asthma, BHR and strict asthma were significant even after the most stringent correction for the number of markers and the number of phenotypes analyzed (<0.0031). An intronic polymorphism (+6651C/T) also showed significant associations with asthma (P=0.0302) atopic asthma (P=0.0131), BHR (P=0.0249) and strict asthma (P=0.0261). In the Danish families, an intronic asthma (P=0.0348), BHR (P=0.0033) and strict asthma (P=0.0381). The results of haplotype analyses supported the ones of the single SNP analyses. Thus, we demonstrated significant evidence of association between polymorphisms in PTGDR with asthma phenotypes in the two Caucasian populations.

Upon information and belief, GSK has analyzed non-coding polymorphisms in PTGDR in a manner that infringed upon claims of the '179 Patent.

77. Upon information and belief, GSK had actual knowledge of the '179 Patent during times relevant to this action through at least its research, development and/or patent application activities

E. HOLOGIC

78. Upon information and belief, in July of 2008 Hologic acquired Third Wave Technologies, which "develops and markets molecular diagnostic reagents for a wide variety of

DNA and RNA analysis applications based on its proprietary Invader chemistry." In 2008, nine weeks of sales attributed to Third Wave diagnostic products was approximately $5.9 million. In 2009, revenue attributed to Third Wave diagnostic products was approximately $37.1 million. One of these diagnostic product lines is sold under the name Invader.

79. Upon information and belief, the Invader chemistry involves two simultaneous reactions. In the primary reaction, a probe and an Invader oligonucleotide anneal to a DNA target sequence of interest. If a mutation or variant is present, a one base overlapping nucleotide structure is cleaved and released as a flap. This reaction is repeated such that the number of flaps released is related to the amount of the target sequence of interest in the sample, which offers a quantitative detection of the genes present in the sample. In the secondary reaction, the flaps attach to a fluorescent resonance energy transfer cassette. Once the flap attaches and the one base overlapping nucleotide is recognized, it releases a fluorescent signal that can be detected with a multi-well fluorometer. The Invader technology has been used to infringe at least one claim of the '179 Patent.

80. The Invader chemistry is used in several products offered by Hologic, including InPlex CF, Life Science Research Kit, Chromosome Specific Panels, Invader Whole Genome Screening Panels, Low Density Genome-wide Panel, Higher Density SNP Panel, Invader UGT1A1 Molecular Assay, and through Hologic AgBio services, which include SNP genotyping.

81. By way of example only, the Invader chemistry used in the InPlex CF test kits detects and identifies mutations and variants in the cystic fibrosis transmembrane conductance regulator gene, including mutations and variants recommended for detection by the 2004

American College of Medical Genetics. Many of these mutations and variants are found in non-coding DNA regions.

82. Hologic AgBio has also offered services using InvaderPlus technology, including SNP genotyping, transgene detection and infections disease applications. Hologic has also offered the Universal Invader product, which allows researchers to design reactions that use the Invader chemistry. Both InvaderPLUS and Universal Invader involve PCR amplification followed by the Invader chemistry reaction and can be used and, upon information and belief, have been used to conduct methods covered by the '179 Patent.

83. Upon information and belief, Hologic had actual knowledge of the '179 Patent during times relevant to this action through at least its research, development and/or patent application activities.

F. MERIAL

84. Merial has offered a series of genetic tests for DNA markers associated with quality traits in beef and dairy cattle under the trade name "Igenity." According to Merial's marketing materials, "Igenity helps you understand and manage the potential for animals to perform and transmit traits of economic importance." The Igenity DNA marker profile includes numerous non-coding DNA markers associated with genes responsible for these traits. Merial's analysis of these non-coding DNA markers has thus infringed upon claims of the '179 Patent.

85. By way of example only, the Igenity TenderGENE tests for three DNA markers including two SNPs in the calpain gene (CAPN 316 and CAPN 4751) and one in the calpastatin gene (UoG-CAST 1). These genetic markers are associated with meat tenderness. At least the CAPN 4751 and UoG-CAST 1 markers are located in non-coding regions. Upon information

and belief, Merial amplified DNA with a primer pair spanning a DNA sequence containing these non-coding markers. Merial's analysis of these markers thus infringed upon claims of the '179 Patent.

86. Also, by way of example only, Merial has tested for markers associated with the leptin gene, a gene associated with appetite and metabolism and the propensity for meat to marble. The analysis included several non-coding DNA markers. More specifically, Merial's International Patent Application No. WO 2006/096427 A2 ("the '427 Publication") relates to identification of liptin gene polymorphisms and their use in determining genotype/phenotype association in live stock. Three polymorphisms, UASMS 1, UASMS 2, and UASMS 3, are identified in the '427 Publication as being located in promoter or non-coding DNA regions. The '427 Publication also describes the primer pair sequences for the amplification of DNA sequences containing these non-coding markers. Merial's analysis of these markers thus infringed upon claims of the '179 Patent.

87. Also, by way of example only, in the publication entitled "Polymorphisms In Two Positional Candidate Genes In The Bovine Chromosome 14 Are Associated With Carcass Merit In Beef Cattle," presented at the Plant & Animal Genomes XV Conference held January 13-17, 2007 in San Diego, California, Merial states:

> Nine unique polymorphism were identified in DECR1, including 4 exonic SNPs and 4 unique polymorphisms were identified in the CBFA2T1 gene, all of which are intronic. . . . Two of the exonic polymorphisms produced amino acid composition changes from isoleucine to valine and valine to methionine. The latter appears to be located in a conserved region where important catalytic reactions occur.

In the publication entitled "Polymorphisms In The Bovine Fibroblast Growth Factor 8 (FGF8) Gene Are Associated With Carcass Quality And Growth Traits In Beef Cattle," presented at the

Plant & Animal Genomes XV Conference held January 13-17, 2007 in San Diego, California, Merial states:

> In this experiment, 464 animals from an experimental composite line comprised of Angus, Charolais and Hybrid steers were sequenced for FGF8 introns and exons (NW_930497.1). Four unique polymorphisms were identified, two exonic and two intronic. Single locus and haplotype association analysis . . . were carried out resulting in a number of significant associations with carcass quality and growth traits in beef cattle; including carcass lean meat yield %, ultrasound marbling and birth weight.

In the publication entitled "Genetic And Phenotypic Relationships Of Serum Leptin Concentration With Performance, Feed Efficiency, And Carcass Merit Of Feedlot Cattle," J. Animal Science, pp 1-30, Nkrumah JD et al. (2007), Merial states:

> Mutations in the leptin gene or its promoter are associated with differences in serum leptin concentrations and other economically relevant traits in beef and dairy cattle. Indeed, polymorphisms in the bovine leptin promoter have been shown to have strong associations with serum leptin concentrations as well as body fatness.

88. Since the first offering of its Ingenity tests through the expiration of the '179 Patent, Merial added numerous DNA markers to its Igenity profile. Upon information and belief, many of those markers are located in non-coding DNA regions. Upon information and belief, Merial used DNA amplification to analyze these non-coding DNA markers and to detect the genes responsible for the associated traits of economic importance. These activities thus infringed upon claims of the '179 Patent.

89. Upon information and belief, Merial had actual knowledge of the '179 Patent during times relevant to this action through at least its research, development and/or patent application activities.

G. NAVIGENICS

90. Navigenics was founded in 2006 and began offering services for sale in 2008.

91. In November of 2007, Navigenics filed U.S. Patent Application 12/516,915, which was National Stage Entry of PCT/US07/86138, which was a continuation of U.S. Patent Application 11/781,679 filed July 23, 2007. U.S. Application 12/516,915 published as U.S. Publication No. 2010/0293130 ("the '130 Publication") and describes "methods of determining a Genetic Composite Index score by assessing the association between an individual's genotype and at least one disease or condition. The assessment comprises comparing an individual's genomic profile with a database of medically relevant genetic variations that have been established to associate with at least one disease or condition."

92. The method outlined in the '130 Publication utilizes the method of at least one claim of the '179 Patent. Specifically, but by way of example only, the '130 Publication describes a method of analyzing a DNA sample for genetic predispositions by collecting a sample from an individual, isolating DNA in the sample, amplifying the isolated DNA, analyzing the amplified or isolated DNA, and comparing the analyzed or isolated DNA to known polymorphisms associated with a specific phenotype. Examples of the phenotype and associated genes are located in Table 1 of the '130 Publication and the locations of SNPs associated with a phenotype can be found in Figure 22. At least some of the SNPs analyzed using the method of the '130 Publication are in the coding, i.e., "functional" regions, while others are in the non-coding, i.e., "non-functional" regions, of a gene. Specifically, the '130 Publication states: "A functional SNP has an effect on a cellular function, thereby resulting in a phenotype, whereas a non-functional SNP is silent in function, but may be in linkage disequilibrium with a functional SNP . . ." and

I. THE PARTIES

1. Plaintiff GTG is an Australian corporation with a principal place of business in Victoria, Australia.

2. Upon information and belief, Agilent is a corporation organized and existing under the laws of the state of Delaware, with its principal place of business located at 5301 Stevens Creel Boulevard, Santa Clara, California 95051. Agilent can be served with process through its registered agent, The Corporation Trust Company, Corporation Trust Center, 1209 Orange Street, Wilmington, Delaware 19801.

3. Upon information and belief, Bristol-Myers is a corporation organized and existing under the laws of the state of Delaware, with its principal place of business located at 345 Park Avenue, New York, New York 10154. Bristol-Myers can be served with process through its registered agent, The Corporation Trust Company, Corporation Trust Center, 1209 Orange Street, Wilmington, Delaware 19801.

4. Upon information and belief, ESTA is a corporation organized and existing under the laws of the state of Colorado, with its principal place of business located at 1821 Vista View Drive, Longmont, Colorado 80504. ESTA can be served with process through its registered agent, National Corporate Research, Ltd., 12649 West Warren Avenue, Lakewood, Colorado 80228.

5. Upon information and belief, GSK is a company organized and existing under the laws of the United Kingdom, with its principal place of business in the United States located at One Franklin Place, 200 North 16th Street, Philadelphia, Pennsylvania 19106. GSK can be

this can act as a marker for particular traits. Upon information and belief, Navigenics has provided one or more genotyping and genomic services that utilize the methods set forth in the '130 Publication.

93. Upon information and belief, Navigenics has offered at least two genotyping and genomic testing services. The services are marketed to health care providers or directly to individuals through the Navigenics website. The first service, offered as Navigenics Annual Insight for $499, tests an individual's DNA for a number of possible genetic predispositions, including breast cancer, prostate cancer, colon cancer and heart disease. SNPs related to breast cancer, specifically SNP rs3817198 of the LSP1 gene, are known to be in a non-coding region of the gene.

94. Navigenics has also offered genotyping and genomic testing for additional genomic predispositions, including abdominal aneurysm, Alzheimer's disease, atrial fibrillation, brain aneurysm, Celiac disease, Crohn's disease, deep vein thrombosis, diabetes (type 2), glaucoma, Graves' disease, heart attack, hemochromatosis (HFE-related), lactose intolerance, lung cancer, lupus, macular degeneration, melanoma, multiple sclerosis, obesity, osteoarthritis, psoriasis, restless legs syndrome, rheumatoid arthritis, sarcoidosis, and stomach cancer (diffuse). As recently as April of 2009, Navigenics offered these services, marketed as Navigenics Health Compass, for approximately $2,499 and a subscription to provide ongoing assessments based on new information that can be renewed annually. Upon information and belief, at least some of the SNPs analyzed to determine genomic predispositions using the Navigenics Health Compass occur in the non-coding region of a gene. Navigenics has also offered testing services to analyze an individual's medication response predispositions to Abacavir, beta blocker, carbamazepine,

clopidogrel, floxacillin, fluorouracil, Irinotecan, simvastatin, statins, succinylcholine, thiopurines and Warfarin.

95. Upon information and belief, Navigenics' services analyzed DNA using two possible techniques. The Affy6.0 genotyping platform was used if an association between a SNP and a phenotype was known in the literature and if the SNP could be tested directly (the exact SNP is represented on the array) or indirectly (a tag SNP is present on the array). By way of example only, the SNP used to test for the phenotype in the LSP1 gene related to breast cancer was tested directly by Navigenics using the array following an amplification step. Once analyzed, a genetic risk was combined with other risk factors to generate a Genetic Composite Index ("GCI") score. The GCI is a qualitative estimate of the association of a condition with combined effect of a set of SNPs. The GCI also takes into account known risk factors and other information. The results were presented through Navigenics' secure website and could be shared with the individual's physician.

96. Upon information and belief, prior to early 2009, Navigenics utilized a CLIA compliant laboratory operated by Affymetrix to perform analysis on its DNA samples. In early 2009, Navigenics acquired the CLIA compliant laboratory from Affymetrix and began performing testing for itself.

97. Upon information and belief, Navigenics had actual knowledge of the '179 Patent during times relevant to this action through at least its research, development and/or patent application activities.

H. NEOGEN

98. Neogen is a manufacturer and supplier of food and animal safety products. Its business operates in two divisions – food safety and animal safety. Neogen acquired GeneSeek, Inc. ("GeneSeek") in 2010. GeneSeek's DNA testing services have been incorporated into Neogen's diagnostic testing portfolio under its animal safety division and is directed and controlled by Neogen.

99. GeneSeek is a commercial agricultural genetics laboratory, providing agri-genomic services to research and development and commercial industries. These services include genotyping and gene mapping from sample processing through to data analysis and evaluation, and SNP profiling, marker-assisted selection, identity and diagnostics testing. GeneSeek's marketing materials list alpaca, cattle, canine, goat, horse, swine and sheep as well as maize, rice, soybean and wheat plant species as among the species that it has conducted such testing.

100. GeneSeek maintains service testing facilities in Lincoln, Nebraska that hold a range of platform technologies used to perform its agri-genomic services. These include the Sequenom MassARRAY, Li-Cor DNA Sequence Analyzer and Illumina GoldenGate and Infinium platforms.

101. According to GeneSeek: "with our technical platforms we can handle any project, from a few SNPs (single nucleotide polymorphisms) on thousands of samples to a million SNPs on a few samples. We can process any sample type including hair, blood, tissue and more. We also provide clinical veterinary diagnostics for trait and disease markers and for pathogen detection using quantitative real-time PCR and ELISA. . . . For 12 years we have been the trusted

leader in providing high-throughput SNP and microsatellite genotyping services to the agricultural research and business communities."

102. GeneSeek has performed SNP profiling on Illumina products such as:

Bovine 3K Net Merit Panel 3072 SNP panel

Bovine SNP50 BeadChip – 54,609 informative SNP markers

BovineHD – High density genotyping with greater than 777,000 SNP markers

CanineHD – High density genotyping with greater than 170,000 SNP markers

PorcineSNP60 BeadChip – 62,163 informative SNP markers

OvineSNP50 BeadChip – 54,241 informative SNP markers

EquineSNP50 BeadChip – 54,602 informative SNP markers

Maize SNP50 BeadChip – 56,110 informative SNP markers

Mouse Custom 9K BeadChip

103. SNP profiling using Illumina products detects and analyzes many non-coding DNA markers. By way of example only, the "PorcineSNP60 BeadChip features more than 62,000 evenly spaced SNPs across the entire porcine genome." Since more than 95% of the pig genome is non-coding DNA, many of the probes which target "evenly spaced polymorphic SNPs" are located in non-coding regions. The use of these Illumina products thus infringed upon claims of the '179 Patent.

104. Upon information and belief, GeneSeek utilized DNA amplification as a part of its testing services. By way of example only, GeneSeek states in its marketing materials: "GeneSeek can provide genotyping services for . . . whole genome scans or marker assisted selection . . . Genotyping from plant samples that allow high throughput genotyping at very low

cost. From one or two small leaf disc punches, we are able to analyze your target of interest using standard PCR, real-time PCR, SNPs or microsatellite markers."

105. Also by way of example only, GeneSeek has performed sequencing and microsatellite analysis using the Li-Cor DNA Sequence Analyzer. This platform utilizes PCR amplification of DNA to prepare samples for analysis. Upon information and belief, GeneSeek's sequencing and microsatellite analysis included analysis of markers in non-coding regions. Thus, these activities infringed upon claims of the '179 Patent.

106. Also, by way of example only, GeneSeek's identity and diagnostics portfolio includes "Seek-Gain: Total Gain" and "Seek-Gain: Animal Gain" tests which detect and analyze the non-coding A/G variant at position +179 in the 5' untranslated region of the CCKAR gene and C/T variation at position 576 in intron 6 of the HMGA1 gene. According to GeneSeek, the "cholecystokinin type A receptor (CCKAR) genetic test is associated with physiological control of feed intake, ~5% higher daily feed intake, 3% higher daily gain, and 3% fewer days to reach 180kg, when compared to homozygotes for the A-variant" and the "high mobility group AT-hook protein 1 (HMGA1) genetic test is associated with lean mass percentage, growth and back fat in several swine breeds. Producers can test and select animals (T-variant at position 576) which are likely to be leaner and produce offspring that are leaner." Upon information and belief, these testing services infringed upon claims of the '179 Patent.

107. Also, by way of example only, GeneSeek's "Seek-Gain: Total Gain" and "Seek-Gain: Litter Size" tests detect and analyze the non-coding C/T variant in intron 4 of the EPOR gene. According to GeneSeek, there is "a genetic variant in the swine erythropoietin receptor gene associated with uterine capacity and litter size. The favorable genetic variation has

demonstrated an increase in uterine capacity as well as an increase in live births in two different swine populations at USDA – MARC, including the industry-relevant BX population. In a commercial herd, an extra pig per litter was observed when comparing boars that have two copies of the favorable EPOR marker versus boars with zero copies." Upon information and belief, these testing services infringed upon claims of the '179 Patent.

108. Upon information and belief, Neogen had actual knowledge of the '179 Patent during times relevant to this action through at least its research, development and/or patent application activities.

I. PFIZER

109. Pfizer is active in the area of pharmacogenetics. Pfizer acknowledges that the use of pharmacogenetic information can alter the course of its drug development or change the drug labeling for on-shelf pharmaceutical drugs in order to retain FDA approval.

110. Pfizer has actively advocated pharmacogenetic research, both in terms of therapeutic effect as well as adverse effects. Pfizer has also undertaken numerous pharmacogenetic studies (clinical trials) and funds studies to investigate gene polymorphisms associated with disease and drug response.

111. Pfizer's pharmacogenetic activities include the analysis of non-coding DNA markers. By way of example only, and upon information and belief, Pfizer has analyzed non-coding DNA markers in connection with the drugs Camptosar (Irinotecan) and Zoloft (Sertraline) using methods that infringe claims of the '179 Patent.

112. With respect to Irinotecan, Pfizer directly performed genotyping activities in 2005 as well as funded numerous studies undertaken by third parties using the inventions of the '179

Patent. The genotyping test that is related to the drug's metabolism and thus toxicity interrogates a non-coding polymorphism of the multi-allelic UGT1A1 genetic locus. These activities are directly related to the safety of use of Camptosar and therefore sale of the drug.

113. Irinotecan hydrochloride was originally developed in Japan by the Yakult Honsha Company. Licensing rights for clinical development in the U.S. were granted to Pharmacia, whereas similar rights in Europe were granted to Aventis. Irinotecan was first approved in the U.S. for the treatment of metastatic colorectal cancer after failure of first-line treatment with 5-FU. This initial approval was based on tumor response rate data from phase II, uncontrolled studies. Conditional marketing authorization in the U.S. was granted in 1996 under FDA regulations designed to accelerate approval of new and promising drugs for serious or life-threatening illnesses. Subsequently, Aventis completed two European randomized, phase III studies comparing second-line Irinotecan therapy with best supportive care or with infusional 5-FU-based therapy and provided the data from these trials to Pharmacia. The survival advantages associated with Irinotecan use in each of these trials was the basis for full FDA approval for Irinotecan as second-line therapy for patients with metastatic colorectal cancer in September 1998. It was approved as a first-line therapy in April 2000.

114. Pfizer acquired Pharmacia in 2003 for $60 Billion comprising assets related to Irinotecan in the U.S. and others. Pfizer then acquired the European rights for Irinotecan from Aventis in 2004 for $620 Million. Prior to patent expiration, Irinotecan was Pfizer's major cancer treatment drug with global revenues of $969 Million in 2007. Pfizer lost exclusivity for Irinotecan in February 2008 and July 2009, in U.S. and Europe, respectively. Currently, Pfizer's global revenue from Irinotecan is $117 Million.

115. The UGT1A1*28 allele is a promoter polymorphism reported to effect drug efficacy of Irinotecan. Pfizer conducted a clinical trial entitled "Toxicity/Benefit Ratio Optimization of Chemotherapy in Colorectal Cancer (CRC) Patients by Determination of Individual Genotypic Determinants" in June 2005 and completed the trial in December 2008. The study involved genotyping patients for the UGT1A1 polymorphisms prior to first administration of Irinotecan.

116. The FDA recommended label changes to Irinotecan to include UGT1A1 genetic information in July 2005. In conjunction with the label changes, the FDA simultaneously approved the first commercial kit offered by Third Wave Technologies for genotyping the UGT1A1 polymorphism. Subsequently, there was an increase in both the number of laboratories offering UGT1A1 genotyping as well as availability of related reagents and kits.

117. Upon information and belief, Pfizer has (and/or has directed others to have) amplified DNA with a primer pair spanning a DNA sequence containing the UGT1A1*28 polymorphism which Pfizer has associated with increased risk for neutropenia. Indeed, Pfizer has reported in prescribing information that "UGT1A1 activity is reduced in individuals with genetic polymorphisms that lead to reduced enzyme activity such as the UGT1A1*28 polymorphism. Approximately 10% of the North American population is homozygous for the UGT1A1*28 allele. In a prospective study, in which Irinotecan was administered as a single-agent on a once-every-3-week schedule, patients who were homozygous for UGT1A1*28 had a higher exposure to SN-38 than patients with the wild-type UGT1A1 allele. . . . Individuals who are homozygous for the UGT1A1*28 allele are at increased risk for neutropenia following initiation of CAMPTOSAR treatment. A reduced initial dose should be considered for patients

known to be homozygous for the UGT1A1*28 allele." The analysis of this non-coding DNA marker in this manner thus infringed upon claims of the '179 Patent.

118. With respect to Sertraline, Pfizer has also performed genotyping activities that relate to the inventions of the '179 Patent. The genotyping test that is related to the drug's metabolism and thus toxicity interrogates a non-coding polymorphism (5HTTLPR) of the multi allelic SLC6A4 genetic locus. These activities are directly related to the safety of use of Zoloft and therefore sale of the drug.

119. Zoloft was one of Pfizer's blockbuster drugs generating $2.11 Billion in 2006. It is used to treat major depressive disorder, panic disorder, obsessive-compulsive disorder (OCD) in adults and children, post-traumatic stress disorder (PTSD), premenstrual dysphoric disorder (PMDD) and social anxiety disorder (SAD). Zoloft is approved for acute and long-term use in all of these indications, with the exception of PMDD. The drug went off patent in June 2006.

120. In 2006, Pfizer funded the study "Serotonin Transporter Polymorphisms and Clinical Response to Sertraline Across Ethnicities," which investigated the "relationship between clinical response, adverse effects, Sertraline (SERT) plasma concentrations and the genetic polymorphism of the serotonin transporter gene-linked polymorphic region (5HTTLPR)".

121. Upon information and belief, Pfizer has (and/or directed others to have) amplified DNA with a primer pair spanning a DNA sequence containing the 5-HTTLPR polymorphism which Pfizer has associated with genes effecting serotonin responsiveness. Pfizer's analysis of this non-coding DNA marker in this manner thus infringed upon claims of the '179 Patent.

122. Upon information and belief, Pfizer has also performed other genotyping activities that infringed one or more claims of the '179 Patent. These activities were also directly related to the safety and efficacy and thus the development and/or sale of various drugs.

123. By way of example only, Pfizer's International Patent Application No. WO2005/090601 and entitled "Biomarker of Hypertension" ("the '601 Publication") describes the analysis of the -54E3 polymorphism of the GUCY1 A2 gene. The -54E3 polymorphism is an A/G variant which occurs in intron 2 of the GUCY1A2 gene. The '601 Publication describes the use of PCR and other amplification techniques for amplifying genomic DNA samples and analysis of those samples using a number of tools. For example, Claim 5 of the '601 Publication reads:

> A kit for the diagnosis of hypertension or a predisposition to hypertension in a human subject, or for the selection of a human subject likely to respond to treatment with an sGC activator compound, comprising means for identifying the genotype of the -54E3 A/G single nucleotide polymorphism of the human GUCY1 A2 gene, and/or one or more single nucleotide polymorphisms of GUCY1A2 which is/are in linkage disequilibrium therewith, in DNA taken from the subject.

Pfizer's analysis of the -54E3 polymorphism by this methodology infringed upon claims of the '179 Patent.

124. Also by way of example only, Pfizer's U.S. Patent Publication No. 2010/0324356 and entitled "Methods for Improving Genetic Profiles of Dairy Animals and Products" and which was filed on December 17, 2007, describes the use of DNA amplification and analysis methods to perform marker assisted selection for dairy cattle. These activities infringed claims of the '179 Patent.

served with process through its registered agent, Corporation Service Company, 2711 Centerville Road, Suite 400, Wilmington, Delaware 19808.

6. Upon information and belief, Hologic is a corporation organized and existing under the laws of the state of Delaware, with its principal place of business located at 35 Crosby Drive, Bedford, Massachusetts 01730. Hologic can be served with process through its registered agent, Corporation Service Company, 2711 Centerville Road, Suite 400, Wilmington, Delaware 19808.

7. Upon information and belief, Merial is a limited liability organized and existing under the laws of the state of Delaware, with its principal place of business located at 3239 Satellite Boulevard, Duluth, Georgia 30096. Merial is a joint venture between Merck & Co. and Sanofi-Aventis U.S. Merial can be served with process through its registered agent, The Corporation Trust Company, Corporation Trust Center, 1209 Orange Street Wilmington, Delaware 19801.

8. Upon information and belief, Navigenics is a corporation organized and existing under the laws of the state of Delaware, with its principal place of business located at 1001 East Hillsdale Boulevard, Suite 550, Foster City, California 94404. Navigenics can be served with process through its registered agent, Corporation Service Company, 2711 Centerville Road, Suite 400, Wilmington, Delaware 19808.

9. Upon information and belief, Neogen is a corporation organized and existing under the laws of the state of Michigan, with its principal place of business located at 2620 south Cleveland Avenue, Suite 100, St. Joseph, Michigan 49085. Neogen can be served with process through its registered agent, James L. Herbert, Jr., 620 Lesher Place, Lansing, Michigan 48912.

125. Also by way of example only, Pfizer's International Publication No. WO 2005/031341 and entitled "Methods for Predicting Development of Insulin Resistance" ("the '341 Publication") describes the analysis of the -359 polymorphism of the P110β gene using PCR amplification techniques for amplifying genomic DNA samples. In addition, the '341 Publication describes: "In one aspect of any of the methods of the invention, the step of determining whether the DNA of subject comprises a particular P110β allele can be performed using a nucleic acid molecule that specifically binds a P110β nucleic acid molecule. Preferably, the P110β allele comprises detecting a polymorphism in a transcriptional regulatory region, in further preferred aspects, the methods of the invention comprise determining whether the DNA of an individual comprises a T or a C at position 100 of SEQ ID NO 1, or at position -359 (position 359 upstream from the start codon) of the P110β gene. This may thus comprise determining whether the genomic DNA of an individual comprises a P110β allele, whether mRNA obtained from an individual comprises a P110β allele." These activities infringed claims of the '179 Patent.

126. Upon information and belief, Pfizer had actual knowledge of the '179 Patent during times relevant to this action through at least its research, development and/or patent application activities.

J. 454

127. In January of 2007, 454 began offering for sale the Genomic Sequencer FLX system ("GS FLX"). 454 was acquired by Roche Diagnostics ("Roche") in March of 2007. Upon information and belief, 454 began using and testing the Genomic Sequencer Junior system ("GS Junior") at least as early as 2009. Both the GS FLX and GS Junior systems use a range of

kits containing reagents provided by Roche. The use of these systems has infringed at least one claim of the '179 Patent.

128. The GS FLX and GS Junior systems are used to analyze genomic DNA and PCR products. These materials are segmented into 300-800 base pair fragments if necessary. The fragments are immobilized to a DNA capture bead. The fragmented sequence containing capture bead can be amplified using emulsion PCR and analyzed using the systems.

129. By way of example only and upon information and belief, in 2009, sequencing was performed using the GS FLX system in a study by Nejentsev et al. to determine if there was a genetic variation linked to Type 1 Diabetes ("T1D"). The GS FLX system was used to re-sequence genes believed to be associated with T1D. The study analyzed both coding and non-coding regions of the IFIH1 gene, which is multi-allelic. Thus, when used to analyze the non-coding region of the multi-allelic IFIH1 gene by the process described above, use of the GS FLX system infringed at least one claim of the '179 Patent.

130. Upon information and belief, 454 had actual knowledge of the '179 Patent during times relevant to this action through at least its research, development and/or patent application activities.

V. FIRST CLAIM FOR RELIEF
(Patent Infringement – U.S. Patent No. 5,612,179)

131. GTG incorporates by reference each and every allegation in paragraphs 1 through 130 as though fully set forth herein.

132. Defendants have manufactured, made, had made, used, practiced, imported, provided, supplied, distributed, sold, and/or offered for sale products and/or services that infringed one or more claims of the '179 Patent in violation of 35 U.S.C. § 271(a) and/or have

induced direct infringement of the '179 Patent by others by actively instructing, assisting and/or encouraging others to practice one or more of the inventions claimed in the '179 Patent in violation of 35 U.S.C. § 271(b) and/or have contributed to direct infringement of the '179 Patent by others by offering to sell, selling or providing one or more items which constitute a material part of an inventions defined by claims of the '179 Patent, knowing the same to especially made or adapted for use in an infringement of the '179 Patent, which components are not staple articles or commodities of commerce suitable for substantial non-infringing use in violation of 35 U.S.C. § 271(c).

133. One or more of these Defendants' actions in infringing the '179 Patent have been, and are, willful, deliberate and/or in conscious disregard of GTG's rights, making this an exceptional case within the meaning of 35 U.S.C. § 285 and entitling GTG to the award of its attorneys' fees.

134. GTG has been damaged as a result of Defendants' infringing conduct. Defendants are thus liable to GTG in an amount that adequately compensates GTG for such infringement which cannot be less than a reasonable royalty, together with interest and costs as fixed by this Court under 35 U.S.C. § 284.

VI. JURY DEMAND

GTG hereby requests a trial by jury pursuant to Rule 38 of the Federal Rules of Civil Procedure.

VII. PRAYER FOR RELIEF

GTG requests that the Court find in its favor and against Defendants, and that the Court grant GTG the following relief:

A. Judgment that one or more claims of the '179 Patent has been infringed, either literally, and/or under the doctrine of equivalents, by one or more Defendants and/or by others to whose infringement Defendants have contributed and/or by others whose infringement has been induced by Defendants;

B. Judgment that Defendants account for and pay to GTG all damages to and costs incurred by GTG because of Defendants' infringing activities and other conduct complained of herein in an amount not less than a reasonable royalty;

C. That such damages be trebled where allowed by law for a Defendants' willful infringement;

D. That GTG be granted pre-judgment and post-judgment interest on the damages caused to it by reason of Defendants' infringing activities and other conduct complained of herein;

E. That this Court declare this an exceptional case and award GTG its reasonable attorney's fees and costs in accordance with 35 U.S.C. § 285; and

F. That GTG be granted such other and further relief as the court may deem just and proper under the circumstances.

Respectfully submitted,

Dated: May 25, 2011

By: s/ Benjamin B. Lieb

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ATTORNEYS FOR PLAINTIFF

10. Upon information and belief, Pfizer is a corporation organized and existing under the laws of the state of Delaware, with its principal place of business located at 235 East 42nd Street, New York, New York 10017-5755. Pfizer can be served with process through its registered agent, The Corporation Trust Company, Corporation Trust Center, 1209 Orange Street, Wilmington, Delaware 19801.

11. 454 is organized and existing under the laws of the state of Delaware with its principal place of business located at 1 Commercial Street, Branford, Connecticut, 06405. 454 can be served with process through its registered agent The Corporation Trust Company, Corporation Trust Center 1209 Orange Street, Wilmington, Delaware 19801.

II. JURISDICTION AND VENUE

12. This Court has exclusive jurisdiction of this action for patent infringement pursuant to 28 U.S.C. § 1338(a).

13. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a).

14. Venue is proper in this judicial district pursuant to 28 U.S.C. §§ 1391 and 1400.

15. Upon information and belief, Defendants each have minimum contacts with this judicial district such that this forum is a fair and reasonable one. Defendants have each committed such purposeful acts and/or transactions in Colorado that they reasonably knew and/or expected that they could be hauled into court as a future consequence of such activity. Upon information and belief, Defendants have also transacted and/or, at the time of the filing of this Complaint, are transacting business within the District of Colorado. For these reasons,

personal jurisdiction exists over all Defendants and venue over this action is proper in this Court under 28 U.S.C. §§ 1391(b) and (c) and 28 U.S.C. § 1400(b).

III. THE PATENT-IN-SUIT

16. On March 18, 1997, United States Patent No. 5,612,179 ("the '179 Patent") was duly and legally issued for an "Intron Sequence Analysis Method for Detection of Adjacent Locus Alleles as Haplotypes." A true and correct copy of the '179 Patent is attached as Exhibit A.

17. GTG is the owner of the '179 Patent with the exclusive right to enforce and collect damages for infringement of the '179 Patent during all relevant time periods.

18. The '179 Patent generally relates to methods of analysis of non-coding DNA sequences.

19. The Abstract of the '179 Patent relevantly provides:

> The present invention provides a method for detection of at least one allele of a genetic locus and can be used to provide direct determination of the haplotype. The method comprises amplifying genomic DNA with a primer pair that spans an intron sequence and defines a DNA sequence in genetic linkage with an allele to be detected. The primer-defined DNA sequence contains a sufficient number of intron sequence nucleotides to characterize the allele. Genomic DNA is amplified to produce an amplified DNA sequence characteristic of the allele. The amplified DNA sequence is analyzed to detect the presence of a genetic variation in the amplified DNA sequence such as a change in the length of the sequence, gain or loss of a restriction site or substitution of a nucleotide. The variation is characteristic of the allele to be detected and can be used to detect remote alleles.

20. Independent Claims 1 and 26 of the '179 Patent read:

> 1. A method for detection of at least one coding region allele of a multi-allelic genetic locus comprising: a) amplifying genomic DNA with a primer pair that spans a non-coding region sequence, said primer pair defining a DNA sequence which is in genetic linkage with said genetic locus and contains a sufficient number of non-coding region sequence nucleotides to produce an

amplified DNA sequence characteristic of said allele; and b) analyzing the amplified DNA sequence to detect the allele.

26. A DNA analysis method for determining coding region alleles of a multi-allelic genetic locus comprising identifying sequence polymorphisms characteristic of the alleles, wherein said sequence polymorphisms characteristic of the alleles are present in a non-coding region sequence, said non-coding region sequence being not more than about two kilobases in length.

21. The '179 Patent is presumed valid and enforceable pursuant to 35 U.S.C. § 282.

22. The '179 Patent was previously asserted by GTG in the matter of *Genetic Technologies Ltd. v. Applera Corp.*, Case No. C 03-1316-PJH, in the United States District for the Northern District of California (the "Applera Action"). The Applera Action was ultimately settled with Applera Corporation taking a license to the '179 Patent, among others.

23. The '179 Patent was the subject of a declaratory judgment action initiated by Monsanto in the matter of *Monsanto Company v. Genetic Technologies Ltd.*, Case No. 06-cv-00989-HEA, in the United States District Court for the Eastern District of Missouri, Eastern Division (the "Monsanto Action"). That Monsanto Action was ultimately settled. Monsanto has now taken three licenses to the '179 Patent, among others.

24. The '179 Patent was most recently asserted by GTG in the matter of *Genetic Technologies Ltd. v. Beckman Coulter, Inc., et al*, Case No. 10-cv-0069-BBC, in the United States District Court for the Western District of Wisconsin (the "Beckman Coulter Action"). The Beckman Coulter Action was resolved with at least Beckman Coulter, Inc., Gen-Probe, Inc., Interleukin Genetics Incorporated, Molecular Pathology Laboratory Network, Inc., Orchid Cellmark, Inc., Pioneer Hi-Bred International, Inc., and Sunrise Medical Laboratories, Inc. all taking a license to the '179 Patent, among others. GTG has secured over $14.5 million in licensing revenue since the filing of the Beckman Coulter Action in 2010.

25. In addition to the licenses identified in the preceding paragraphs, the '179 Patent and related patents have been licensed to at least the following entities: AgResearch Ltd.; ARUP Laboratories, Inc.; Australian Genome Research Facility Ltd.; Bio Reference Laboratories (subsidiary GeneDx); Bionomics Ltd.; BioSearch Technologies Inc.; Pfizer Animal Health; C Y O'Connor ERADE Village Foundation (incorporating the Immunogenetics Research Foundation and the Institute of Molecular Genetics and Immunology Incorporated); Crop and Food Research Ltd.; DNA Diagnostics Ltd.; General Electric Co. and its subsidiary GE Healthcare Bio-Sciences Corp.; Genosense Diagnostics GmbH; Genzyme Corp.; Innogenetics N.V.; Kimball Genetics, Inc.; Laboratory Corporation of America Holdings, Inc.; Livestock Improvement Corporation Ltd.; MetaMorphix, Inc.; Millennium Pharmaceuticals Inc.; Myriad Genetics, Inc.; Nanogen, Inc.; New Zealand Blood Service; Optigen, L.L.C.; Ovita Ltd.; Perlegen Sciences, Inc.; Prometheus Laboratories Inc.; Qiagen, Inc.; Quest Diagnostics Inc.; Sciona, Inc.; Sequenom, Inc.; Syngenta Crop Protection AG; Thermo Fisher Scientific Inc.; TIB MOLBIOL Syntheselabor GmbH; Tm Bioscience Corporation; Gen-Probe, Inc.; and others.

26. Certain claims of the '179 Patent, including Claim 26, were recently subjected to an ex parte reexamination before the United States Patent and Trademark Office ("USPTO") that was initiated by an unknown entity. On February 4, 2010, the USPTO issued a Notice of Intent to Issue Ex Parte Reexamination Certificate indicating that the subject claims were confirmed as valid without amendment. A true and correct copy of that Reexamination Certificate is attached as Exhibit B.

27. The '179 Patent expired on March 9, 2010. However, GTG remains entitled to collect damages for past infringement occurring during the term of the '179 Patent pursuant to 35 U.S.C. §§ 284 and 286.

IV. DEFENDANTS' INFRINGEMENT

28. Upon information and belief, and as further described below, Defendants have manufactured, made, had made, used, practiced, imported, provided, supplied, distributed, sold, and/or offered for sale products and/or services that infringed one or more claims of the '179 Patent; and/or Defendants have induced and/or contributed to the infringement of one or more of the claims of the '179 Patent by others.

A. AGILENT

29. Agilent acquired Stratagene Corporation ("Stratagene") in June of 2007, and Stratagene became part of Agilent's Bio-Analytical Measurements business group. According to Stratagene marketing materials, "[i]t offers products in various categories, including amplification, cloning, nucleic acid analysis, quantitative PCR, cell biology, microarrays, and protein function and analysis. [Stratagene] also provides software for pathway analysis and microarray data analysis."

30. In 2008, $2.3 billion of Agilent's net revenue was attributed to its Bio-Analytical Measurement business group, which provides "instruments, software, consumables and services that enable customers to identify, quantify and analyze the physical and biological properties of substances and products." In 2009, $2.1 billion of Agilent's net revenue was attributed to its Bio-Analytical Measurement business group. In 2010, $1.5 billion of Agilent's net revenue was attributed to its Life Science business group, which includes "liquid chromatography, mass